

Oral tuberculosis - Current concepts

Supriya Sharma¹, Jyoti Bajpai², Pankaj K. Pathak³, Akshyaya Pradhan⁴,
Priyanka Singh¹, Surya Kant²

¹Department of Oral Pathology and Microbiology, Faculty of Dental Sciences, ²Department of Respiratory Medicine, King George's Medical University (KGMU), Lucknow, Uttar Pradesh, ³Department of Family and Community Medicine, AIIMS, Patna, Bihar, ⁴Department of Cardiology, King George's Medical University, Lucknow, Uttar Pradesh, India

ABSTRACT

Tuberculosis (TB) is a chronic infectious disease that can affect various parts of the body including the oral cavity. It primarily affects the lungs. TB bacilli can spread hematogenously to different parts of the body and this also involves maxilla or mandible. Although oral lesions are infrequent, they are crucial for the early diagnosis and interception of primary TB. Intercepting the disease early will limit the morbidity and mortality of the patients. It becomes the responsibility of the dentist to include TB in the differential diagnosis of suspicious oral lesions to prevent delay in the treatment of the disease. It would not be an exaggeration if the dental identification of the TB lesions has the potential of serving as a significant aid in the first line of control for this hazardous and often fatal disease. This article will also emphasize the advancing role of oral pathologists in making the final diagnosis of this dreaded disease.

Keywords: *Mycobacterium tuberculosis* (Mtb), oral tuberculosis, ulcerative lesion

Introduction

Tuberculosis is a disease characterized by granulomatous lesions caused by *Mycobacterium Tuberculosis* (Mtb). A German scientist Robert Koch discovered the causative organism of TB in 1882. Since time immemorial, it has been a global health problem.^[1] TB has shown a decline in its prevalence globally; however, it is still highly prevalent in Asian countries. One-fourth of the global burden of TB is in India. TB is usually overlooked in the differential diagnosis of oral lesions as it is supposed to be a rare entity. Although oral TB is supposed to be a rare occurrence, it still accounts for 0.5–1% of all tubercular cases. Oral manifestations of TB occur either due to infected sputum or due to hematogenous spread.^[2,3]

TB is an age old disease and has been known to mankind for thousands of years. One can find its description in the oldest

medical literature of India, Egypt, and China. In the ancient literature, TB has been described as kshay rog, phthisis, king's evil, and white plague.

In the Indian system of medicine (the Ayurveda), the treatment of TB has been described as spending time in fresh air and good nutrition. Later on, these three basic principles of treating TB in Ayurveda became the cornerstone of sanatorium treatment. Sanatoria treatment remained the popular treatment modality until 1943 when first antitubercular drug streptomycin was discovered. Later on, a number of other antitubercular drugs, such as thiacetazone, para-aminosalicylic acid, pyrazinamide, and rifampicin, were discovered. With the extensive use of these antitubercular drugs, the problem of TB has been controlled to a large extent, at least in the developed countries. However, the resurgence of TB was also observed in the developed countries since 1981 due to the increasing prevalence of human immunodeficiency virus (HIV). Later on in 1993, World Health Organization declared TB as a global emergency due to an increase in its

Address for correspondence: Dr. Surya Kant,
Department of Respiratory Medicine, King George's Medical
University (KGMU), Lucknow - 226 003, Uttar Pradesh, India.
E-mail: skantpulmed@gmail.com

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_97_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Sharma S, Bajpai J, Pathak PK, Pradhan A, Singh P, Kant S. Oral tuberculosis - Current concepts. J Family Med Prim Care 2019;8:1308-12.

prevalence, its association with HIV, and increasing problem of drug resistance.^[2,3]

Purpose of this review article is to aid in making an early diagnosis of oral TB and also to emphasize the increasing role of oral pathologists in making the final diagnosis of this dreaded disease.

Global Burden of the Disease and Prevalence

According to WHO (2016), TB represents an important public health concern nowadays, with approximately 10.4 million occurrences of new cases and may cause 1.7 million deaths per year globally. As per the report of WHO (2015), the incidence rate of TB is about 10.4 million and cause 1.5 million deaths per year globally.^[3,4]

Burden of TB in India

In India, the prevalence rate of TB is 3.2 million while 2.7 million new cases of TB were reported per year and about 4 lakhs 23 thousand deaths had been reported due to TB per year.^[4] Oral TB is considered as a rare disease and its prevalence ranges from 0.5% to 1% of all tubercular cases.

Risk factors related TB

Pulmonary TB (PTB) is a multibacillary disease and sputum of these patients contains a larger number of bacilli. On the other hand, oral TB is a paucibacillary disease and concentration of acid-fast bacilli (AFB) is significantly less in saliva. Local factors in the oral cavity, which may be contributing to decreased susceptibility for the development of oral TB, are the resistance of striated muscles to bacterial invasion, saprophytes, and thickness of protective epithelial covering. Another very important factor for oral TB susceptibility is a breach of the oral mucosa, which may lead to the colonization of bacteria. Poor oral hygiene, local trauma, leukoplakia, and irritation by clove chewing can also be considered as the attributing factors.^[5-7]

Immunocompromised states, such as HIV, diabetes mellitus, malnutrition, malignancies prolonged corticosteroids therapy, and chronic renal failure, may also pose a threat to the development of TB. General conditions, such as overcrowding, addiction to alcohol or smoking, poor ventilation and sunlight source, early marriage, and repeated pregnancies at small intervals, are also the risk factors for TB.^[1,8,9]

Oral manifestations of TB

Tuberculous lesions of the oral cavity do occur but are relatively uncommon. Oral TB lesions may be either primary or secondary in occurrence. Primary lesions are uncommon, seen in younger patients often associated with enlarged cervical lymph nodes. Secondary oral TB usually coexists with pulmonary disease, may occur in all age groups; however, middle-aged and older people are more likely involved. The most likely route of inoculation is the entry of organisms in the sputum and, from there, entry into the mucosal tissue through a small break in the surface. It

is possible that the organisms may be carried to the oral tissues by a hematogenous route, to be deposited in the submucosa, and subsequently to proliferate and ulcerate the overlying mucosa.

In case of oral TB, the tongue is the most commonly affected site in various forms, such as ulcers, nodule, fissures, plaques, or vesicles. However, it can affect buccal mucosa, gingiva, tongue, lips, palate, palatine tonsil, and floor of the mouth [Figures 1 and 2].^[13] The salivary glands, tonsils, and uvula are also involved frequently. Primary oral TB usually involves gingival and presents as a diffuse, hyperemic, nodular, or papillary proliferation of the gingival tissues. It is usually associated with regional lymphadenopathy. Primary gingival involvement is more common in children and adolescents than in adults.^[10-13] It usually presents as a single painless indolent ulcer that progressively extends from the gingival margin to the depths of the adjacent vestibule and is often associated with enlarged cervical lymph nodes. They may be single or multiple, painful or painless and usually appear as irregular, well-circumscribed ulcer with surrounding erythema without indurations and satellite lesions are commonly found. When oral TB arises as a primary lesion, an ulcer is the most prevalent presentation generally developing along the lateral margins of the tongue that ease against rough, sharp, or broken teeth or at the site of other irritants. Patients with oral tubercular lesions often have a history of preexisting trauma. Any area of chronic irritation or inflammation may favor localization of the *Mycobacterium* associated with the disease. Deep tubercular ulcers of the tongue are typical in appearance with a thick mucus material at the base. These tongue lesions are characterized by severe unremitting and progressive pain that profoundly interferes with proper nutrition and rest. Classically, tubercular ulcers of the tongue may involve the tip, lateral margins, the midline, and base of the tongue. The clinical aspect and microscopic features confirmed the appearance of tubercular ulcers as irregular, pale, and indolent with inverted margins and granulations on the floor with sloughing tissue.

The usual presentation of secondary TB is an irregular, superficial, or deep, painful ulcer that tends to increase slowly



Figure 1: Tuberculous ulcer on tongue^[13]



Figure 2: Ulcer in the buccal vestibule^[13]

in size. It is frequently found in areas of trauma and may be mistaken clinically for a simple traumatic ulcer or even carcinoma. Occasional mucosal lesions show swelling, granular, modular, or fissured lesions, but no obvious clinical ulcerations.^[13,14] TB may also involve the bone of maxilla or mandible. One common mode of entry for the microorganism is into an area of periapical inflammation by way of the bloodstream. It is also possible that these microorganisms may enter the periapical tissues by direct immigration through the pulp chamber and root canal of a tooth with an open cavity. The lesion produced is essentially a tuberculous periapical granuloma or tuberculoma; diffuse involvement of the maxilla or the mandible may also occur, usually by hematogenous spread of the infection, but sometimes by direct extension or even after tooth extraction. Tuberculous osteomyelitis frequently occurs in the later stages of the disease and has an unfavorable prognosis.^[15]

Role of an oral pathologist

On the basis of the clinical presentation, it is very difficult for clinicians to make the diagnosis of oral TB. While evaluating a chronic, indurated ulcer, clinicians should consider the differential diagnosis of the infectious processes, such as primary syphilis, deep fungal diseases, and noninfectious processes, such as chronic traumatic ulcer and squamous cell carcinoma. Oral ulcer should further be evaluated by excisional biopsy and its histopathological examination, AFB smear microscopy, AFB culture, bacterial, and fungal culture, etc. Due to the paucity of AFB in the oral lesions, the sensitivity of AFB examination is very low. In various studies, AFB smear positivity in a various biopsy specimen of the oral lesion has been found around 7.8%.^[3] Typically, histopathology of the biopsy specimen shows a classical caseating granuloma with central necrosis and is surrounded by epithelioid cells, Langhan's type of giant cells, and lymphocytes infiltration. However, in immunocompromised conditions such as acquired immunodeficiency syndrome, there may be a noncaseating granuloma. A biopsy of an oral lesion is confirmatory but in the majority of the cases, a single biopsy may not suffice because the granulomatous changes may not be

evident in early lesions. Sometimes repeated biopsies may be required and fine needle aspiration cytology may also be tried if a biopsy is not possible. Mantoux skin test and chest X-ray should be done to rule out the systemic TB.

In case of diagnostic dilemma correlation of history, the clinical and radiological examination should be done. Laboratory confirmation and thorough histopathological examination are most essential for the diagnosis, with the culture of microorganisms taken as the absolute proof of the disease. However, molecular tests such as line probe assay, nucleic acid amplification test, and polymerase chain reaction, and microbiological tests such as culture, mycobacterial growth indicator tube, and BACTEC are considered to be the best tools for the diagnosis of TB.

The differential diagnosis for oral lesions of TB

Oral lesions of TB are nonspecific in their clinical presentation and often are overlooked in differential diagnosis, especially when oral lesions are present before systemic symptoms become apparent. With the increasing numbers of TB cases, unusual forms of the disease in the oral cavity are more likely to occur and be misdiagnosed. Hence, doctors and dentists should be aware of the oral lesions of TB and should consider them in the differential diagnosis of suspicious oral ulcers.

The aphthous ulcers, traumatic ulcers, syphilitic ulcers, and malignancy, including primary squamous cell carcinoma, lymphoma, and metastases are the differential diagnosis of the tubercular ulcer of the oral cavity. As reported earlier, the most likely clinical diagnosis is that of squamous cell carcinoma, in which biopsy is mandatory. It is most likely that TB is only considered when the histological specimen reveals a granulomatous lesion. This would then lead to consideration of other orofacial granulomatous conditions such as sarcoidosis, Crohn's disease, the deep mycoses, cat-scratch disease, foreign-body reactions, tertiary syphilis, and Melkersson–Rosenthal syndrome.^[10]

Treatment

The treatment of oral TB lesions is identical as systemic TB. Currently, the most effective regimens require a combination of 4 drugs [isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (ETO)] administered daily for the first 2 months, followed by an additional 4 months with 3 drugs (INH, RIF and ethambutol). The difficulty of this regimen prompted the WHO to launch a new global strategy for TB control known as “Directly Observed Therapy, Short course” (DOTS) in 1997. The central component of this strategy is a direct observation by trained personnel, which secures both patient compliance with the drug regimen and decreases the likelihood of drug resistance.

The management of TB is strenuous because of the two primary factors: persistence and resistance. In spite of the fact that antibiotics are accessible, *Mtb* is extremely persistent, possibly because the bacterium encourages chronic

inflammation that sequesters it inside the tissues, defending it against drug exposure. Thus, drug treatment must be extended to completely damage the bacterium and prevent relapse. Drug resistance is the result of genetic mutations that cause a heritable loss of drug susceptibility. Even though resistance to a single drug does not render therapy unsuccessful, multidrug-resistant strains make TB much more expensive and difficult to treat. For this reason, they require newer and more effective drugs that achieve multiple goals in improving TB controls that are imperative.^[16,17] There are two types of resistance commonly observed in the context of TB: multidrug resistant TB (MDR) and extensively drug resistant (XDR). MDR-TB is described as *Mtb* resistant to the most effective first-line anti-TB drugs, isoniazid, and rifampicin, whereas XDR-TB has additional multidrug resistance to the most potent second-line agents, injectable drugs (aminoglycosides and/or cyclic polypeptides-capreomycin, amikacin, and kanamycin), and fluoroquinolones.^[18]

Potential new agents should decrease the duration of treatment, have a satisfactory tolerability outline, be active against MDR/XDR TB, be of use in HIV-infected patients with TB, and be active against latent TB.^[19-21]

Precautions for dental healthcare professionals

Clinical dental practice suffers from the vulnerability for transmission of miscellaneous infections from patient to dentist, patient to patient, as well as dentist to patient due to close proximity to the nasal and oral cavities of the patient. Thus, a barrier should be generated to inhibit the transmission of infections and to perform the clinical procedures secure from the threat of cross infections. A thorough history of TB should prompt the dental practitioner to recognize whether the person is an active case under treatment, the active case without treatment, or formerly infected but presently disease free. The nontreated active cases stand maximum risk to the dental healthcare personnel.^[22]

Dental healthcare professionals are at the uniform risk of getting exposed to TB by the means of splatter, aerosols, or infected blood. As various severe diseases are air-borne, blood-borne, or can extend through the contact of other body fluids, and it is not possible to know which certain patients are infected, so it is pertinent to avoid direct contact with body fluids, blood, and mucous membranes. Dental treatment for those with active TB should be restricted to urgent and necessary procedures.

High levels of operatory disinfection and instrument sterilization should be provided. For recognized active TB patients, TB isolation rooms that are properly equipped rooms with functional air evacuation, negatively pressured correlative to the corridors, with air either debilitated to the outside or HEPA-filtered if recirculation is mandatory, with high volume suction are designated for carrying out any procedure to reduce the aerosol production. Portable suction should be eluded as they recirculate

air. Rubber dams can be accustomed to minimize aerosol contact, nevertheless if coughing occurs it should not be used.

Proper sterilization procedures, personal protective gears (head caps, eye shields, face masks, gloves, and surgical gowns), and maintenance of proper hand hygiene should be followed. Dental healthcare personnel should use particulate face masks because standard surgical face masks do not protect against TB transmission. If the mask becomes wet, it should be changed at regular intervals, interappointments (between patients), and intra-appointments (during patient's treatment). Other oral instruments and handpieces should be cleaned and autoclaved routinely. The aim of the dental infection-control program is to bestow a safe working environment that minimizes the risk of both healthcare-related infections between patients and occupational exposures among dental team members.^[23]

Discussion

In India, a large number of dentists and consultants in otolaryngology have restricted experience with the TB of the upper aerodigestive tract since its oral lesions are indefinite in its clinical appearance and are often excluded from the differential diagnosis. This is very pertinent in cases where oral lesions are existing before the systemic symptoms become apparent.^[24]

Oral tubercular lesions can be either primary or secondary to PTB, with secondary lesions being more prevalent. Most affected sites for these lesions are tongue, palate, buccal mucosa, lips, gingiva, and floor of the mouth. The diagnosis of these lesions generally becomes strenuous as different lesions like a traumatic ulcer, syphilitic ulcer, or squamous cell carcinoma, aphthous ulcer are suggested in the first thought, in observer differential diagnosis before inclusion of TB, leading to misdiagnosis.^[25,26]

However, laboratory investigations have the principal role that provides definite evidence and confirms the disease. The diagnosis of TB is confirmed by the presence of AFB in the specimen, or more likely by the culture of tuberculous bacilli. The culture of sputum, clinical, and radiological examination is other supportive mode of confirmatory diagnosis. A procedure of taking diverse deeper biopsies can also ultimately make the job obvious. Compulsory steps should be followed to exclude systemic TB like a chest X-ray and a Mantoux skin test.

The treatment of TB require a combination of 4 drugs (INH, RIF, PZA, and ETO) administered daily for the first 2 months, followed by an additional 4 months with 3 drugs (INH, RIF, and ETO) for the complete elimination of the tubercular lesions.

TB is global health pandemic with huge economic ramifications. It can affect people of all ages, sex, and race. Oral TB though rare and poses a challenge for diagnosis but certainly offers a window to contain TB at a stage when it is localized. Hence, early management and diagnosis of oral TB is going to have public health implications as it can be considered a sort of primary

prevention for late sequelae of TB. Oral problems are often perceived as of being of miniscule health hazard and more often than not treated by home remedies or at best by primary care physicians. Hence, the primary care physician with his adequate knowledge of the disease can serve as an effective barrier to curb its spread. Moreover, even after specialist consultation, the patient often has a tendency to revisit the primary care physician because of physical or emotional proximity.

Conclusion

Oral tubercular lesions are rare, difficult to diagnose, and pose a potential infectious hazard to dental personnel engaged in the treatment. So, each and every persistent and atypical oral lesion must be examined carefully to intercept and prevent the disease early. Intercepting the disease early will advance the morbidity and mortality of the patients. So, it becomes the responsibility of the dentist to include TB in the differential diagnosis of suspicious oral lesions to avoid delay in the treatment of this disease.

Acknowledgments

The authors would like to thank Faculty of Dental Sciences, King George's Medical University and also the Department of Oral Pathology and Microbiology for their immense support and cooperation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Rao VG, Muniyandi M, Bhat J, Yadav R, Sharma R. Research on tuberculosis in tribal areas in India: A systematic review. *Indian J Tuberc* 2018;65:8-14.
- Kant S, Srivastava K, Singh S, Tiwari S, Rizvi SHA. Update history of tuberculosis. *LMJ* 2011;1:2-11.
- Jain P, Jain I. Oral manifestations of tuberculosis: Step towards early diagnosis. *J Clin Diagn Res* 2014;8:18-21.
- WHO: 2017. Global Tuberculosis Report 2016. Geneva, Switzerland: World Health Organization; 2017.
- Pekiner FN, Erseven G, Borahan MO, Gumru B. Natural barrier in primary tuberculosis inoculation: Oral mucous membrane. *Int J Tuberc Lung Dis* 2006;10:1418.
- Emmanuelli JL. Infective granulomatous diseases of the head and neck. *Am J Otolaryngol* 1993;14:155-67.
- Ito FA, de Andrade CR, Vargas PA, Jorge J, Lopes MA. Primary tuberculosis of the oral cavity. *Oral Dis* 2005;11:50-3.
- Woods RG, Amerena V, David P, Fan PL, Heydt H, Marianos D, *et al.* Additional precautions for tuberculosis and a self-assessment checklist: *FDI World* 1997;6:10-7.
- Srivastava K, Kant S, Verma A, Dubey A. Tuberculosis: An overview. *Everyman's Sci* 2015;L(2):123-35.
- Von A, Husain A. Oral tuberculosis. *Br Dent J* 2001;190:420-2.
- Sezer B, Zeytinoglu M, Tuncay U, Unal T. Oral mucosal ulceration. A manifestation of previously undiagnosed pulmonary tuberculosis. *J Am Dent Assoc* 2004;135:336-40.
- Ebenezer J, Samuel R, Mathew GC, Koshy S, Chacko RK, Jesudason MV, *et al.* Primary oral tuberculosis: Report of two cases. *Indian J Dent Res* 2006;17:41-4.
- Kapoor S, Gandhi S, Gandhi N, Singh I. Oral manifestations of tuberculosis. *Chrimed J Health Res* 2014;1:11-4.
- Tripathi A, Deora A, Kant A, Sharma S. Oral manifestations of tuberculosis. *LMJ* 2011;1:42-4.
- Kant S, Sharma S, Verma SK, Singh R. Isolated tubercular osteomyelitis of the mandible. *Int J Orthop Surg* 2008;9:1-4.
- Sacchetti JC, Rubin EJ, Freundlich JS. Drugs versus bugs: In pursuit of the persistent predator *Mycobacterium tuberculosis*. *Nat Rev Microbiol* 2008;6:41-52.
- Spigelman MK. New tuberculosis therapeutics: A growing pipeline. *J Infect Dis* 2007;196:28-34.
- Kant S, Maurya AK, Kushwaha RAS, Nag VL, Prasad R. Multi-drug resistant tuberculosis: An iatrogenic problem. *Bio Sci Trends* 2010;4:39-47.
- Chan B, Khadem TM, Brown J. A review of tuberculosis: Focus on bedaquiline. *Am J Health Syst Pharm* 2013;70:1984-94.
- Van den Boogaard J, Kibiki GS, Kisanga ER, Boeree MJ, Aarnoutse RE. New drugs against tuberculosis: Problems, progress, and evaluation of agents in clinical development. *Antimicrob Agents Chemother* 2008;53:849-62.
- Shivakoti R, Sharma D, Mamoon G, Pham K. Association of HIV infection with extrapulmonary tuberculosis: A systematic review. *Infection* 2017;45:11-21.
- Popescu MR, Plesea IE, Olaru M, Strâmbu IR, Fronie AI, Petrescu IO, *et al.* Morphological aspects in tuberculosis of oral cavity—Our experience and a review of the literature attempt. *Rom J Morphol Embryol* 2015;56:967-87.
- Blumberg HM, Burman WJ, Chaisson RE, Daley CL, Etkind SC, Friedman LN, *et al.* American thoracic society, centers for diseases control and prevention, infectious disease society of America. Treatment of tuberculosis. *Am J Resp Crit Care Med* 2003;167:603-62.
- Pandit A. Tuberculosis: A basic discourse. *Apollo Med* 2016;13:86-90.
- Eng HL, Lu SY, Yang CH, Chen WJ. Oral tuberculosis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:415-9.
- Bloom BR, Murray GT. Tuberculosis commentary on a reemergent killer. *Science* 1992;257:1055-64.